

What is claimed is:

1. A polynucleotide comprising a nucleic acid sequence encoding a lysosomal enzyme, a secreted protein, a nuclear protein, or a cytoplasmic protein operably linked to a nucleic acid sequence encoding a protein transduction domain (PTD).
2. The polynucleotide of claim 1, wherein the nucleic acid sequence encodes a lysosomal enzyme.
3. The polynucleotide of claim 2, wherein the lysosomal enzyme is a soluble lysosomal enzyme.
4. The polynucleotide of claim 3, wherein the soluble lysosomal enzyme is  $\beta$ -glucuronidase, pepstatin insensitive protease or palmitoyl protein thioesterase.
5. The polynucleotide of claim 3, wherein the soluble lysosomal enzyme is  $\beta$ -glucuronidase.
6. The polynucleotide of claim 1, wherein the nucleic acid sequence encodes a secreted protein.
7. The polynucleotide of claim 2, wherein the secreted protein is a growth factor or an anti-neoplastic protein.
8. The polynucleotide of claim 7, wherein the growth factor is GDNF, NGF, BDNF, or NT3.
9. The polynucleotide of claim 7, wherein the anti-neoplastic protein is an inhibitor of neovascularization, cell migration, or cell proliferation.

10. The polynucleotide of claim 1, wherein the polynucleotide is a nuclear protein.
11. The polynucleotide of claim 10, wherein the nuclear protein is a transcription factor.
12. The polynucleotide of claim 1, wherein the polynucleotide is a cytoplasmic protein.
13. The polynucleotide of claim 12, wherein the cytoplasmic protein is a cytotoxic agent.
14. The polynucleotide of claim 1, wherein the PTD is Tat PTD.
15. The polynucleotide of claim 14, wherein the Tat PTD is Tat<sub>47-57</sub>.
16. An expression vector comprising a nucleic acid sequence encoding a lysosomal enzyme, a naturally secreted protein, a nuclear protein, or a cytoplasmic protein operably linked to a nucleic acid sequence encoding a PTD.
17. The vector of claim 16, wherein the nucleic acid sequence encodes a lysosomal enzyme.
18. The vector of claim 16, wherein the lysosomal enzyme is a soluble lysosomal enzyme.
19. The vector of claim 18, wherein the soluble lysosomal enzyme is  $\beta$  - glucuronidase, pepstatin insensitive protease or palmitoyl protein thioesterase.
20. The vector of claim 19, wherein the soluble lysosomal enzyme is  $\beta$  - glucuronidase

21. The vector of claim 16, wherein the nucleic acid sequence encodes a secreted protein.
22. The vector of claim 21, wherein the secreted protein is a growth factor or an anti-neoplastic protein.
23. The vector of claim 22, wherein the growth factor is GDNF, NGF, BDNF, or NT3.
24. The vector of claim 22, wherein the anti-neoplastic protein is an inhibitor of neovascularization, cell migration, or cell proliferation.
25. The vector of claim 16, wherein the nucleic acid is a nuclear protein.
26. The vector of claim 25, wherein the nuclear protein is a transcription factor.
27. The vector of claim 16, wherein the nucleic acid is a cytoplasmic protein.
28. The vector of claim 27, wherein the cytoplasmic protein is a cytotoxic agent.
29. The vector of claim 16, wherein the PTD is Tat PTD.
30. The vector of claim 29, wherein the Tat PTD is Tat<sub>47-57</sub>.
31. The vector of claim 16, wherein the vector is an adenoviral vector.
32. The vector of claim 16, wherein the vector is an adeno-associated virus vector.

33. The vector of claim 16, wherein the vector is a recombinant lentivirus or retrovirus vector.

34. A polypeptide comprising a lysosomal enzyme, a naturally secreted protein, a nuclear protein, or a cytoplasmic protein operably linked to a nucleic acid sequence encoding a PTD.

35. The polypeptide of claim 34, wherein the polypeptide is a lysosomal enzyme.

36. The polypeptide of claim 34, wherein the lysosomal enzyme is a soluble lysosomal enzyme.

37. The polypeptide of claim 36, wherein the soluble lysosomal enzyme is  $\beta$ -glucuronidase, pepstatin insensitive protease or palmitoyl protein thioesterase.

38. The polypeptide of claim 36, wherein the soluble lysosomal enzyme is  $\beta$ -glucuronidase

39. The polypeptide of claim 34, wherein the polypeptide is a secreted protein.

40. The polypeptide of claim 39, wherein the secreted protein is a growth factor or an anti-neoplastic protein.

41. The polypeptide of claim 40, wherein the growth factor is GDNF, NGF, BDNF, or NT3.

42. The polypeptide of claim 40, wherein the anti-neoplastic protein is an inhibitor of neovascularization, cell migration, or cell proliferation.

43. The polypeptide of claim 34, wherein the polypeptide is a nuclear protein.

44. The polypeptide of claim 43, wherein the nuclear protein is a transcription factor.

45. The polypeptide of claim 34, wherein the polypeptide is a cytoplasmic protein.

46. The polypeptide of claim 45, wherein the cytoplasmic protein is a cytotoxic agent.

47. The polypeptide of claim 34, wherein the PTD is Tat PTD.

48. The polypeptide of claim 47, wherein the Tat PTD is Tat<sub>47-57</sub>.

49. A mammalian cell comprising the vector of claim 12.

50. The cell of claim 49, wherein the cell is human.

51. The cell of claim 49, wherein the cell is from spleen, kidney, lung, heart, liver or brain.

52. The cell of claim 49, wherein the cell is a stem or progenitor cell.

53. A method of treating a genetic disease or cancer in a mammal comprising administering the polynucleotide of claim 1.

54. The method of claim 53, wherein the mammal is human.

55. The method of claim 53, wherein the genetic disease is a lysosomal storage disease (LSD).

56. The method of claim 55, wherein the LSD is infantile or late infantile ceroid lipofuscinoses, Gaucher, Juvenile Batten, Fabry, MLD, Sanfilippo A, Late Infantile Batten, Hunter, Krabbe, Morquio, Pompe, Niemann-Pick C, Tay-Sachs, Hurler (MPS-I H), Sanfilippo B, Maroteaux-Lamy, Niemann-Pick A, Cystinosis, Hurler-Scheie (MPS-I H/S), Sly Syndrome (MPS VII), Scheie (MPS-I S), Infantile Batten, GM1 Gangliosidosis, Mucopolidosis type II/III, or Sandhoff disease.

57. The method of claim 58, wherein the genetic disease is a neurodegenerative disease.

58. The method of claim 57, wherein the neurodegenerative disease is Huntington's disease, ALS, hereditary spastic hemiplegia, primary lateral sclerosis, spinal muscular atrophy, Kennedy's disease, Alzheimer's disease, a polyglutamine repeat disease, or focal exposure such as Parkinson's disease.

59. A method of treating a genetic disease or cancer in a mammal comprising administering the vector of claim 16.

60. A method of treating a genetic disease or cancer in a mammal comprising administering the polypeptide of claim 34.

61. A method of treating a genetic disease or cancer in a mammal comprising administering the cell of claim 49.

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